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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/599,697	10/05/2006	Jurgen Wagner	PAT033714-US-PCT	2925

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NOVARTIS
CORPORATE INTELLECTUAL PROPERTY
ONE HEALTH PLAZA 101/2
EAST HANOVER, NJ 07936-1080

EXAMINER	
WEBB, WALTER E	

ART UNIT	PAPER NUMBER
1612	

MAIL DATE	DELIVERY MODE
03/01/2011	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/599,697	WAGNER ET AL.	
	Examiner	Art Unit	
	WALTER E. WEBB	1612	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *12/2/2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5 and 15-22* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *5 and 15-22* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *12/2/2010*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicants' arguments, filed 12/2/2010, have been fully considered. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. The following rejections and/or objections are either reiterated or newly applied. They constitute the complete set presently being applied to the instant application.

Claim Rejections - 35 USC § 103

1) Claims 5, 15 and 16 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Heath et al. (US 5,545,636) in view of Bradshaw et al., (Agents Actions 1993).

Response to Argument

Applicant argues that the artisan would not select any PKC beta 1 or 2 inhibitor from Heath for the treatment of organ or transplant rejection or for the prolongation of graft survival since Bradshaw merely teaches that one should use bis-indolymaleimides to study the role of PKC in cellular processes, and that bis-indolymaleimides can be inactive in a whole range of models of acute inflammation (see Remarks at p.7. last paragraph through pg. 8).

This argument is not persuasive.

The test of obviousness is not the express suggestion of the claimed invention in any or all of the references, but what the references taken collectively would suggest to those of ordinary skill in the art presumed to be familiar with them. The artisan would have understood from the teaching of Bradshaw that bis-indolylmaleimides showing a

high degree of selectivity for protein kinase C (PKC) would have been useful for treating a number of PKC mediated disease conditions including transplant rejection, which is specifically discussed in that reference (see Bradshaw at pg. 138). The artisan would have reasonably expected the bis-indolylmaleimides of Heath et al. to be useful for treating the same disease conditions, since the bis-indolylmaleimides of Heath et al. "are useful in the treatment of conditions in which protein kinase C has demonstrated a role in pathology" (see Heath et al. at col. 11, lines 60-63).

Applicant argues further that Bradshaw was published in 1993, i.e. 11 years before the priority date of the present application, which "is certainly more relevant to consider what was known in the art at the time of filing (rather than what was known over a decade before the filing date)" (see Remarks at pg. 8, second paragraph).

This argument is not persuasive

In response to applicant's argument based upon the age of the references, contentions that the reference patents are old are not impressive absent a showing that the art tried and failed to solve the same problem notwithstanding its presumed knowledge of the references. See *In re Wright*, 569 F.2d 1124, 193 USPQ 332 (CCPA 1977). Here applicant provides no showing that the art tired and failed to solve the same problem of administering bis-indolylmaleimides to treat transplant rejection.

Applicant argues that a reference, Baier et al., reflects more accurately the state of the art at the time of applicant's invention and based on Baier et al. the artisan would expect PKC theta to play a key role in transplant rejection.

This argument is not persuasive.

It is not clear how the reference to Baier et al. more accurately reflects the state of the art at the time of applicant's invention since it does not discuss transplant rejection or bis-indolymaleimides. The reference to Baier et al. is merely a review on T cell expressed PKC gene products, their known and/or suspected regulation and cellular effector pathways, as well as physiological functions in T lymphocytes. The references to Heath et al. and Bradshaw more accurately reflect the state of the art at the time of applicant's invention since they discuss bis-indolylmaleimides and transplant rejection.

Applicant argues that the combination of Heath et al. and Baier et al. teach away from the claimed invention since "Heath emphasizes that only one or two PKC isozymes may be involved in a given disease state" and Beier et al. teaches that PKC alpha and theta are involved in the regulation of T cell proliferation (see Remarks at pg. 9, second paragraph).

This argument is not persuasive.

The instant claims are not rejected over Heath et al. in view of Baier et al. Heath et al. teaches that the compounds are useful in the treatment of conditions in which protein kinase C has demonstrated a role in pathology. It would have been obvious to

use the compounds of Heath et al. to treat transplant rejection since transplant rejection has been recognized in the art as a condition in which protein kinase C has demonstrated a role in pathology.

Applicant argues that the Office has yet to identify the rational underpinning to select compound A and compound B from the very large genus of Heath to select prevention or treatment of transplant rejection from Bradshaw.

However, compound A is specifically taught as a preferred species and the artisan would have selected it based on this preference (see Heath et al. at col. 53, Example 68, lines 19-32).

2) Claims 5, 15, 16 and 20-22 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Heath et al. (US 5,545,636) in view of Albert et al., (US 2004/0053949).

Response to Arguments

Applicant argues that given the notable structural differences between the compounds of Heath and Albert, the artisan would not consider the compounds to be equivalent, and that "the activity of the Albert compounds cannot be extrapolated to form any expectation as to the activity of the heath compounds" (see Remarks at pg. 13, first paragraph).

This argument is not persuasive.

The compounds of Heath are protein kinase C inhibitors, which are useful in the treatment of conditions in which protein kinase C has demonstrated a role in pathology. The compounds of Albert are also protein kinsae C inhibitors useful in the treatment of protein kinase C mediated conditions. Heath and Albert also teach treating the same diseases, i.e. Alzhiemer's disease, central nervous system disorders, cardiovascular disease, inflammation, ischemia and cancer (see Albert at pg. 19 paragraph [0245] and Heath at col. 11, lines 60-67). Like the compounds of Heath, the compounds of Albert inhibit the beta isoform of protein kinase C (see Albert at pg. 18, paragraph [0221]). The structural differences between the compounds of Heath and Albert do not appear to vastly alter the function of these compounds, since they inhibit the same isoform of protein kinase C and are useful for treating the same diseases. Albert specifically shows a significant increase in graft survival in an animal model when the animal was administered an indolylmaleimide at a dose of 30 mg/kg/day (see pg. 19, paragraph [0244]). The artisan would reasonably expect the compounds of Heath to be useful for the same purpose.

3) Claims 17-19 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Heath et al. (US 5,545,636) and Albert et al., (US 2004/0053949) in view of Goekjian et al., (Expert Opinion Investigative Drugs 2001).

Response to Arguments

Applicant argues that a skilled person having knowledge of the large structural differences between Ro 32-0432 of Goekjian et al., and compound A would not therefore be led to make any assumptions as to the activity of compound A.

This argument is not persuasive.

Goekjian et al. teaches the use of a PKC inhibitor, Ro 32-0432, having selective inhibition for beta-1 and beta-2 isozymes of PKC, for treating graft-versus-host disease (see pg. 2131, right column, 2nd paragraph for discussion of graft-versus-host disease; see pg. 2128, Table 4 for isozyme selectivity of 32-0432). The compound of Goekjian et al., like the compound of Heath, is a bis-indolylmaleimide. The artisan would reasonably expect the compound of Heath to be useful for the same purpose.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Walter E. Webb whose telephone number is (571) 270-3287. The examiner can normally be reached on 8:00am-4:00pm Mon-Fri EST.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Frederick F. Krass can be reached (571) 272-0580. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Walter E. Webb
/Walter E Webb/
Examiner, Art Unit 1612

/Frederick Krass/
Supervisory Patent Examiner, Art Unit 1612